Acetylation of DNA Polymerase Beta Regulates the Choice of the Base Excision Repair Pathway

Olivia Howald and Lata Balakrishnan

Department of Biology, School of Science, Indiana University Purdue University Indianapolis

Base excision repair (BER) is the main pathway through which base damages are repaired in the cell. Single nucleotide damage can be corrected either through short patch BER (SP-BER), in which the single damaged base is replaced, or long patch BER (LP-BER), in which two or more nucleotides can be replaced. Several proteins are involved in the process including DNA polymerase beta (pol β) and FEN1, both of which are the focus for this study. DNA pol β is a multifunctional protein which contains both polymerase and lyase properties. In LP-BER, pol β displaces the uncleaved 5'dRP moiety into a flap structure which is recognized and cleaved by FEN1 and subsequently ligated by DNA ligase 1. Previous *in vitro* studies show that pol β acetylation reduces lyase activity, requiring repair to proceed via LP-BER. In this study, we determined the effect of *in vitro* acetylation on the enzymatic activities of DNA pol β and FEN1. Both unmodified and acetylated forms of pol β were tested for their synthesis and strand displacement activities. Interestingly, acetylated forms of pol β showed much greater activity at all concentrations versus unmodified forms. Interestingly we also found that FEN1 cleavage activity was increased in reactions containing acetylated pol β compared to the unmodified form due to the increased strand displacement activity of the polymerase. Our results suggest that the acetylated form of DNA pol β more actively participates in LP-BER, creating longer strands of corrected, higher fidelity nucleotides.

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